REMARKS

Claims 15-24, 26, 29-30, 32-38, 40 and 42 are pending in this application. Claims 15-17, 29, 33, 37, 38, 40 and 42 are amended herewith. New dependents Claim 43 and 44 are added herewith.

Amendment of Claims 15-17 and 29

The amendments to Claims 15 and 29 are directed solely to certain punctuation used in the text of the claims. These amendments are being presented in an attempt to use a uniform punctuation approach throughout the entire claim set. No new subject matter is added by virtue of these amendments, and the amendments are not considered to alter the scope of the claims in any way. The amendments to Claims 16 and 17 merely change "or" to "and" so that the Claims recite proper Markush groups.

Amendment of Claims 33, 37 and 38

Claims 33 and 37-38 have been amended to correct inadvertent spelling errors. The amendment to Claim 33 merely replaces two words "neuro inflammation" with a single word "neuroinflammation". The amendments to both Claim 37 and 38 merely replaces "neurohal" with "neuronal".

Amendment of Claim 40

Claim 40 has been amended to fully reflect Applicants' concessions on the restriction requirement issue (as it relates to the definitions for R^1, R^2 and R^3) that were addressed in the previous response. Applicants inadvertently neglected to amend these definitions as part of the previous response, and apologize for the oversight.

Amendment of Claim 42

Claim 42 has been amended to use introductory language having more appropriate antecedent basis in the claim from which it depends.

New Dependent Claims 43 and 44

New dependent Claims 43 and 44 are added herewith. Claim 43 is dependent Claim 15, and further limits the scope of the claim to neuroinflammation associated with AIDS dementia, amyotrophic lateral sclerosis, Creuzfeldt-Jacob disease, Down's syndrome, diffuse Lewy body's disease, Huntington's disease, leukoencephalopathy, multiple sclerosis,

Parkinson's disease, Pick's disease, Alzheimer's disease, stroke, temporary lobe epilepsy and tumors. This subject matter is fully supported in the Specification on pages 1-2, and on page 41, lines 8 to 17. Claim 44 is dependent on claim 43 and further limits the scope of the claim to neuroinflammation associated with multiple sclerosis. As previously set out in their response filed October 6, 2003, Applicants have clearly described the link between neuroinflammation and the diseases associated with microglia activation.

The Examiner's Rejections under 35 U.S.C. §112, 1¶

The Examiner has rejected Claims 15-24, 26, 29, 30, 32-38, 40 and 42 under 35 U.S.C. §112, 1¶ as failing to comply with the enablement requirement. In particular, the Examiner states that "the specification does not reasonably provide enablement for a method of treating a patient suffering from chronic inflammation or a disease associated with chronic inflammation with the instant compounds."

As support for this rejection the Examiner lists the 8 well-known factors set forth in the Federal Circuit decision *In re Wands*, 8 USPQ 2d, 1400 (Fed. Cir. 1988), and appears, in essence, to base the rejection primarily on issues relating to the "*state of the art*" factor, and the "*level of predictability in the art*" factor (also referred to by the Examiner as "factor 3" and "factor 5", respectively) and primarily due to a lack of actual clinical data in the specification establishing the successful treatment patients suffering from chronic inflammation with the compounds of the claimed invention. Applicants base this last statement on the language used by the Examiner in section of the Office Action that provides the "overview" of the position taken (i.e., the specific language following the citation of *Wands* that explains why the facts of the case warrant a rejection):

> "In terms of factor [sic] 3 and 5, the state of the art and the level of predictability in the art [sic] cannot be predicted with any certainty beyond what specific test compounds/compositions and/or additional therapeutic agents should be used and are likely to provide productive results beyond those therapeutic compounds/compositions and/or additional therapeutic agents taught in the specification. There is no indication which compounds where [sic] tested for their effect on microglial activation."

(Office Action at page 3, lines 7- 13). This quoted language, taken together with the language appearing under each *Wands* factor heading used in the Office Action illustrates that the Examiner's concern underlying the rejection is based on the fact that mere *in vitro* test data is

not predictive of which compounds (if any) would ultimately be approved by the FDA as an "effective" medicine to treat chronic inflammation. While probably true in most instances, this facile observation is entirely irrelevant to the analysis of Section 112 as it relates to the **claimed invention**.

Applicants have claimed a method of treating chronic inflammation (Claim 15), and a method of treating disorders associated with microlia activation (Claim 40), by administering a compound of formula II to patients suffering from these disorders. However, no limitation of the claims require that these methods actually satisfy the FDA standards required for ultimate marketing approval. While such regulatory approval is required for any pharmaceutical invention to ever reach the market (if it ever does—most do not), it is **not** required as a part of the enablement requirement of Section 112 of the Patent Act. Indeed, there is no provision in the Patent Act that requires claimed inventions to be commercially viable. Commercial *viability* is completely irrelevant to the question of *patentability*.

Based on the measured activity of the disclosed compounds, Applicants have drafted Claims to encompass what they believe to be the diseases and disorders reasonably expected to be treatable by inhibitors of microglia activation. As case law makes abundantly clear, unless the Examiner can offer actual proof to the contrary, the Examiner must accept the Applicants' statement as true that they reasonably expect compounds within the scope of the claims to serve as potential therapeutic agents for the claimed diseases and disorders. The Examiner has failed to provide such proof based on objective evidence, and instead merely points to the general proposition that various disorders have (or could have) various causative agents and involve different cellular mechanisms. This basic observation is insufficient to carry the burden of properly supporting the 35 U.S.C. §112, 1¶ rejection. The Examiner has failed to offer any specific proof that the compounds within the scope of the claims would not be expected to exhibit **any** therapeutic value.

The Examiner's rejection appears to be largely (if not wholly) based on the improper use of the "*safe and effective*" standard under the Federal Food, Drug and Cosmestic Act, rather than the proper "*utility*" standard under the Patent Act. These two very different standards are not interchangeable. Indeed, the improper interchanging of these different standards was squarely rejected by the U.S. Court of Appeals for the Federal Circuit in *In re Brana*, 34 USPQ 2d 1436 (Fed. Cir. 1995).

As stated above, the Applicants' Specification must be taken to be in compliance with §112 unless the Examiner provides a supported reason to doubt otherwise:

> "A specification ... *must* be taken as in compliance with the enabling requirement of the first paragraph of §112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support."

In re Brana, 34 USPQ 2d at 1441 (emphasis in original). As in the present case, the decision in *In re Brana* involved the USPTO improperly second-guessing the utility of claimed pharmaceutical compounds on the basis that pre-clinical testing of the compounds does not provide any definitive proof that the compounds could actually be used to treat any disorder. The Court clearly rejected this approach stating:

> "FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as cancer."

In re Brana, 34 USPQ 2d at 1443 (citations omitted, emphasis added). As made perfectly clear by this decision, patent claims to pharmaceutical inventions can cover "potential cures" – not just compounds where safety and efficacy has been clearly and definitively established. *Id.* As in *Brana*, where the basis for the USPTO's §112, 1¶ rejection is merely a vague asserted doubt in the predictive nature of the Applicants basis for claiming utility: "applicants should not have been required to substantiate their presumptively correct disclosure to avoid a rejection under the first paragraph of §112." *In re Brana* at 1441.

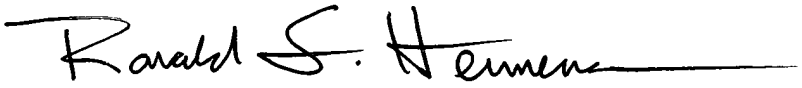
Applicants have provided more than a reasonable link between the activity of the claimed compounds, and the claimed utilities of these compounds. Notwithstanding the Examiner's general observation as to the predictability of finding effective drugs for various disorders, Applicants have sufficiently enabled the pending method claims under the standard set forth in *In re Brana.* As *In re Brana* makes abundantly clear the need for ongoing research and development does not negate enablement in the context of pharmaceutical inventions. Indeed such ongoing experimentation is typical in the pharmaceutical industry, and (while

substantial in both terms of quantity and time), does not properly qualify as "undue" experimentation within the pharmaceutical art. Those of skill in the art know quite well the required steps to take before any invention can be granted FDA marketing approval.

Conclusion

In view of the above amendments and remarks, Applicants respectfully request that the Examiner withdraw the §112, 1¶ rejection and pass all pending claims to allowance.

Respectfully submitted,



Ronald S. Hermenau
Attorney for Applicants
Registration No. 34,620

Berlex Pharmaceuticals
Corporate Patents
2600 Hilltop Drive
P.O. Box 4099
Richmond, California 94804-0099
Telephone: (510) 669-4483
Fax: (510) 262-7095
E-mail: ron_hermenau@berlex.com

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